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Metabolic Modeling of the Last Universal Common Ancestor

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Background: The origin and diversity of life on earth are intimately linked to metabolic processes. Recent advancements in our understanding of the metabolic capability of early life [1] enables systematic investigations into primordial metabolism. A framework that incorporates geobiochemical, environmental, and metabolic constraints would allow for a more complete understanding of early biological systems.

Approach: Constraint-based modeling of biochemical networks coupled with flux-balance analysis has a long history of contextualizing cellular metabolism [2]. Using recent assessments of early metabolic capabilities [1][3], we construct a metabolic model of a primordial organism that could be representative of the last universal common ancestor (LUCA). A core set of possible metabolic reactions derived from phylogenetic analysis [1] served as a scaffold to build the base metabolic network. Gaps in the base network were filled using a database of candidate reactions and existing modeling algorithms. Geobiochemical phenomena such as hydrothermal vents will be integrated with the model to investigate interactions with the environment.

Significance: A systems biology view of LUCA enables the quantitative evaluation of competing hypotheses concerning the origins of metabolic capabilities. The inclusion of mathematically-defined geobiochemical constraints represents a significant leap forward in systems biology. Ultimately, this model can serve as a framework to investigate the interface between early living systems with geochemical environments.

References:

[1] Weiss MC et. al (2016) *Nature Microbiology* 1:16116. [2] O'Brien EJ et. al. (2015). *Cell* 161:971-987. [3] Goldford et. al. (2017). *Cell* 168:1126-1134

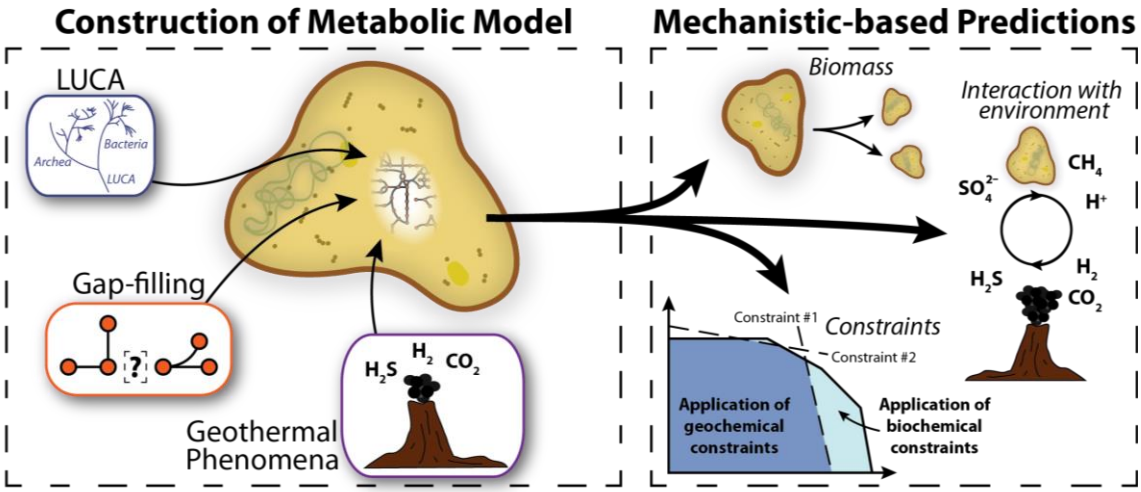

Figure 1 – Conceptual framework for the generation and applications of the metabolic model.